10

1. A pharmaceutical composition comprising an orally administrable effective unit solid dosage of a primary N-hydroxylamine or a pharmaceutically acceptable salt thereof and substantially free of a nitrone corresponding to the hydroxylamine, wherein the hydroxylamine has the general formula,

NHOHCR<sub>1</sub>R<sub>2</sub>R<sub>3</sub>

wherein  $R_1$ ,  $R_2$  and  $R_3$  are independently selected from: substituted or unsubstituted (C0-C10) alkyl, alkenyl, alkynyl, aryl, oxyl, acyl, carboxyl, amino, nitro, nitroso, oxime, hydrazone, azo, thiol, sulfonyl and halide.

- 2. A composition according to claim 1 wherein the dosage is from 100ug to 1g.
  - 3. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is selected from unsubstituted (C0-C10) alkyl, alkenyl and alkynyl.
  - 4. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is selected from unsubstituted (C0-C18) alkyl, cycloalkyl, alkenyl and alkynyl, and the R is selected from:  $CH_3$ -( $CH_2$ )<sub>n1</sub>, ( $CH_3$ -( $CH_2$ )<sub>n2</sub>-)<sub>2</sub> CH, ( $CH_3$ -( $CH_2$ )<sub>n2</sub>-)<sub>3</sub>, cyclopentyl, cyclohexyl, ( $CH_2$ =CH- $CH_2$ )<sub>n3</sub> and (CH=C- $CH_2$ -)<sub>n3</sub>, wherein n1 = 1 to 18, n2 = 1 to 17 and n3 = 1 to 3.
  - 5. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is selected from unsubstituted (C0-C10) alkyl, alkenyl and alkynyl, and the hydroxylamine is selected from:

50

N-methylhydroxylamine,	N-(n-decahexyl)hydroxylamine,
N-ethylhydroxylamine,	N-(n-decaoctyl)hydroxylamine,
N-n-propylhydroxylamine,	N-isopropylhydroxylamine,
N-(n-butyl) hydroxylamine,	N-sec-butylhydroxylamine,
N-(n-pentyl)hydroxylamine,	N-tert-butylhydroxylamine,
N-(n-hexyl)hydroxlamine,	N-cyclohexylhydroxylamine,
N-(n-heptyl)hydroxylamine,	N-cyclopentylhydroxylamine,
N-(n-octyl)hydroxylamine,	N-(2-propene)hydroxylamine,
N-(n-nonyl)hydroxylamine,	N-(3-butene)hydroxylamine,
N-(n-decyl)hydroxylamine,	N-(2-propyne)hydroxylamine and
N-(n-dodecyl)hydroxylamine,	N-(3-butyne)hydroxylamine.

- 6. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted aryl.
- 7. A composition according to claim 1, wherein at least one R of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted aryl, and the R is selected from: mono, di, or tri methyl, methoxy, halo, nitro, amino, hydroxyl and substituted or unsubstituted phenyl, naphthyl, anthryl, phenanthryl, pyridyl, quinolinyl, imidazolyl, benzoxazolyl, pyrrolyl, furanyl, piperidinolyl and tetrahydrofuranyl.
- 8. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted aryl, and the hydroxylamine is selected from:

N-benzylhydroxylamine,	N-(1,3-diaminobenzyl)hydroxylamine,
N-(n-nitrobenzyl)hydroxylamine,	N-(1,3-hydroxybenzyl)hydroxylamine,
N-(n-methylbenzyl)hydroxylamine,	N-(2,4-diaminobenzyl)hydroxylamine,
N-(n-chlorobenzyl)hydroxylamine,	N-(2,4-dihydroxybenzyl)hydroxylamine,
N-(n-aminobenzyl)hydroxylamine,	Imidazole-2-methylhydroxylamine and
N-(n-hydroxybenzyl)hydroxylamine,	Benzoxazole-2-methylhydroxylamine,

wherein n is selected from 1, 2, 3, 4, 5 and 6.

5

10

25

30

9. A composition according to claim 1, wherein at least one R of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted

11. A composition according to claim 1, wherein at least one R of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C0-C18)alkyl hydroxyl or arylhydroxyl and the hydroxylamine is selected from:

N-(hydroxymethyl)hydroxylamine,	N-(methoxymethyl)hydroxylamine,
N-(2-hydroxyethyl)hydroxylamine,	N-(methoxyethyl)hydroxylamine,
N-(3-hydroxypropyl)hydroxylamine,	N-(methoxyisopropyl)hydroxylamine,
N-(4-hydroxybutyl)hydroxylamine,	N-(benzyloxymethyl)hydroxylamine and
N-(6-hydroxyhexyl)hydroxylamine,	N-(4-hydroxymethylbenzyl)hydroxylamine.
N-(12-hydroxydodecyl)hdyroxylamine,	

- 12. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted (C0-C18) alkylcarboxyl or arylcarboxyl.
- 13. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted (C0-C18) alkyl or aryl carboxyl and the R is selected from carboxyalkyls and benzyl.
- 14. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted alkyl (C0-C18) or arylcarboxyl and the hydroxylamine is selected from:

other getting the programment of the second of the second

25

5

10

52

N-(carboxymethyl)hydroxylamine,	N-(5-carboxypentyl) hydroxylamine,
N-(2-carboxyethyl)hydroxylamine,	N-(6-carboxyhexyl)hydroxylamine,
N-(3-carboxypropyl)hydroxylamine,	N-(4-carboxybenzyl)hydroxylamine and
N-(4-carboxybutyl)hydroxylamine,	N-(12-carboxydodecyl)hydroxylamine

- 15. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted (C0-C18) ester.
- 16. A composition according to claim 1, wherein at least one R of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C0-C18) ester and the R is selected from alkyl (C0 C18) and aryl esters.
  - 17. A composition according to claim 1, wherein at least one R of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted alkyl (C0-C18) or arylesters and the hydroxylamine is selected from:
  - N-(acetyloxymethyl)hydroxylamine,
  - N-(acetyloxyethyl)hydroxylamine,

10

ոնս կան կում այի պարտ այի այլ այլ այլ այր այր կարեր այլ կարեր կարեր և այլ կարեր այլ կարեր և այլ կարեր և

- N-(acetyloxypropyl)hydroxylamine,
- N-(propylcarbonyloxy)methylhydroxylamine,
- N-(butylcarboxyloxy)methylhydroxylamine,
- N-(tert-butyloxycarboxyl)methylhdyroxylamine,
- N-(benzyloxycarbonyl)methylhydroxylamine,
- N-(phenyloxycarbonyl)methylhydroxylamine,
- N-(3-pyridyloxycarbonyl)methylhydroxylamine and
- N-(benzoxazol-5-carbonyloxy)methylhydroxylamine.
  - 18. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted (C0-C18) carbonyl.
- 19. A composition according to claim 1, wherein at least one R of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted carbonyl and the R is selected from alkyl (C0 C18) carbonyls and aryl carbonyls.

	111111	: \$
	1	1000
	(lend)	The Party
	June 1	114
15	1,111	Ğ
	11820	÷
	ilinia.	ij
	Same?	
	111	
	ralia.	÷
	1000	100
	Henry	
20	ř	·新州·斯·斯·
۷.		ill il
	ndin	

10

20. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted alkyl (C0-C18) or arylcarbonyls and the hydroxylamine is selected from:

N-(acetyl)methylhydroxylamine,	N-(phenylcarbonyl)methylhydroxylamine
N-(ethylcarbonyl)methylhydroxylamine,	and
N-(butylcarbonyl)methylhydroxylamine,	N-(benzylcarbonyl)methylhydroxylamine.

- 21. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted alkyl(C0-C18) or aryl amino.
- 22. A composition according to claim 1, wherein at least one R of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted alkyl (C0-C18) or aryl amino and the R is selected from primary alkyl amine selected from methylamine, ethylamine, propylamine, butylamine and hexylamine, secondary amine selected from dimethylamine, diethylamine and dipropylamine, tertiary amine selected from trimethyl and trietylamine, and quarternary amine selected from tetramethyl and tetra-ethylammonium salts.
- 23. A composition according to claim 1, wherein at least one R of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted alkyl(C0-C18) or aryl amine and the hydroxylamine is selected from:

N-aminomethylhydroxylamine,

N-(2-aminoethyl)hydroxlamine,

N-(N-methylamino)methylhydroxylamine,

N-(N,N-dimethylamino)methylhydroxylamine,

25 N-(N,N,N-trimethylammonium)methylhydroxylamine,

N-(3-aminopropyl)hydroxylamine,

N-(6-aminohexyl)hydroxylamine,

N-(4-aminobenzyl)hydroxylamine,

Hydroxylamine -1-methylpyridinium and

30 Hydroxylamine-1-methylquinolinium.

24. A composition according to claim 1, wherein at least one R of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is

5

10

- 35. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted alkyl(C0-C18) or aryl nitro and the R is selected from alkylnitro selected from nitromethyl, nitroethyl, nitropropyl, nitrobutyl, nitropentyl, nitrohexyl and nitrobenzyl, and arylnitro selected from nitrophenyl and nitronaphthyl.
- 26. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted alkyl (C0-C18) or aryl nitro and the hydroxylamine is selected from:

N-(nitromethyl)hydroxylamine,	N-(5-nitropentyl)hydroxylamine,
N-(2-nitroethyl)hydroxylamine,	N-(6-nitrohexyl)hydroxylamine,
N-(3-nitropropyl)hydroxylamine,	N-(4-nitrobenzyl)hydroxylamine and
N-(4-nitrobutyl)hydroxylamine,	N-(2,4-dinitrobenzyl)hydroxylamine.

- 27. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted (C0-C18) nitroso.
- 28. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted (C0-C18) nitroso and the R is selected from aliphatic nitrosoamines and aromatic nitroso.
- 29. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted nitroso (C0-C18) and the hydroxylamine is selected from:
- N-(N-methyl-N-nitroso-amino)methyl hydroxylamine,
- N-(N-methyl-N-nitroso-2-amino)ethylhydroxylamine,
- N-(N-methyl-N-nitroso-3-amino)propylhydroxylamine and
- N-(p-nitroso)benzylhydroxylamine.
- 30. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted oxime.

10

- 31. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted (C0-C18) oxime and the R is selected from: acetaldoxime, propionaldoxime, butanaldoxime and benzaldoxime.
- 32. A composition according to claim 1, wherein at least one R of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted oxime (C0-C18) and the hydroxylamine is selected from:

Acetaldoxime-3-hydroxylamine,	Butanaldoxime-5-hydroxylamine and
Propionaldoxime-4-hydroxylamine,	(4-benzaldoxime)1-methylhydroxylamine.

- 33. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted (C0-C10) hydrazone.
  - 34. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted (C0-C10) hydrazone and the R is selected from: acetaldehyde hydrazone, propanaldehyde hydrazone, butanaldehyde hydrazone and phenylhydrazone.
  - 35. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted hydrazone (C0-C10) and the hydroxylamine is selected from

1-hydroxylamine-acetaldehyde hydrazone,	1-hydroxylamine-butanaldehyde hydrazone
1-hydroxylamine-propanaldehyde	and
hydrazone,	1-hydroxylamine-benzylaldehyde
	hydrazone.

- 36. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted azo.
- 37. A composition according to claim 1, wherein at least one R of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted azo and the R is selected from: azobenzene, p-(phenylazo)benzyl and p-diazobenzyl.
- 38. A composition according to claim 1, wherein at least one R of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted azo and the hydroxylamine is selected from:

ally that that must shall that with and

And And may and age as

25

30

15

- 39. A composition according to claim 1, wherein at least one R of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C0-C18) thiol.
  - 40. A composition according to claim 1, wherein at least one R of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C0-C18) thiol and the R is selected from (C0-C18) alkylthiol selected from methyl, ethyl, propyl, butyl, pentyl and hexyl thiol, and arylthiol selected from thiophenol and benzylthiol
  - 41. A composition according to claim 1, wherein at least one R of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C0-C18) thiol and the hydroxylamine is selected from:

N-(thiomethyl)hydroxylamine,	N-(3-thiopropyl)hydroxylamine and
N-(2-thioethyl)hydroxylamine,	N-(p-sulfhydryl)benzylhydroxylamine.

- 42. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted (C0-C18) sulfonic acid.
- 43. A composition according to claim 1, wherein at least one R of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C0-C18) sulfonic acid and the R is selected from methanesulfonic acid, ethanesulfonic acid, propanesulfonic acid, butanesulfonic acid and ptoluenesulfonic acid.
- 44. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted (C0-C18) sulfonic acid and the hydroxylamine is selected from:

1-hydroxylamine-methanesulfonic acid,	1-hydroxylamine-butane-4-sulfonic acid
1-hydroxylamine-ethane-2-sulfonic acid,	and
1-hydroxylamine-propane-3-sulfonic acid,	N-(p-sulfobenzyl)hydroxylamine.

30

5

10

- 45. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is halide.
- 46. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is halide and the R is selected from F, Cl, Br and I.

47. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is halide and the hydroxylamine is selected from:

N-(chloromethyl)hydroxylamine,	N-(4-chlorobutyl)hydroxylamine,
N-(bromomethyl)hydroxylamine,	N-(p-chlorobenzyl)hydroxylamine,
N-(2-chloroethyl)hydroxylamine,	N-(p-fluorobenzyl)hydroxylamine and
N-(3-chloropropyl)hydroxylamine,	N-(p-iodobenzyl)hydroxylamine.

- 48. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted hydroxylamine
- 49. A composition according to claim 1, wherein at least one R of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted hydroxylamine and R is selected from N-methylhydroxylamine, N-ethylhydroxylamine, N-propylhydroxylamine N-butylhydroxylamine, N-pentylhydroxylamine, and N-benzylhydroxylamine
- 50. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is is substituted or unsubstituted hydroxylamine and the hydroxylamine is selected from:

Bis-methylhydroxylamine,	Bis-(3-propyl)hydroxylamine and
Bis-(2-ethyl)hydroxylamine,	Bis-benzylhdyroxylamine

- 51. A composition according to claim 1, wherein at least one R of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C0-C18) phosphoester
- 52. A composition according to claim 1, wherein at least one R of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted (C0-C18) phosphoester and the R is selected from: dimethylphosphate, diethylphosphate, dipropylphosphate and benzylphosphate.

5

54. A composition according to claim 1, wherein the nitrone is less than 1% (wt/wt) of the hydroxylamine in the composition.

55. A pharmaceutical composition according to claim 1 packaged with a label identifying the primary N-hydroxylamine and prescribing a pharmaceutical use thereof.

ոն դժականի անհամահան անհամահան հում հում հում հում հում ունե անհամահ

- 56. A pharmaceutical composition according to claim 1 packaged with a label identifying the primary N-hydroxylamine and prescribing a pharmaceutical use thereof and the use is other than oncological.
- 57. A pharmaceutical composition according to claim 1 packaged with a label identifying the primary N-hydroxylamine and prescribing a pharmaceutical use thereof and the use comprises reducing oxidative damage or delaying senescence.

25

58. A composition according to claim 1 further comprising an effective amount of a carnitine.

30

59. A method for reducing oxidative damage to, or delaying senescence of a cell comprising the step of contacting a cell subject to or at risk of undesirable oxidative damage or senescence with a composition according to claim 1.

identifying a cell as subject to or at risk of undesirable oxidative damage or senescence; and

contacting the cell with a composition comprising an effective amount of a primary hydroxylamine and substantially free of a nitrone corresponding to the hydroxylamine.

- 61. A method according to claim 60, wherein the cell is contained in other than a cancerous host.
- 62. A method for screening for primary N-hydroxylamines which reduce oxidative damage to, or delay senescence of cells, comprising the steps of:

contacting cells with a candidate primary N-hydroxylamine under conditions whereby, but for the presence of the hydroxylamine, the cells present a reference amount of oxidative damage or senescence;

detecting post-treatment amounts of oxidative damage or senescence of the cells; wherein a lesser amount of post-treatment than reference amounts of oxidative damage or senescence indicates that the hydroxylamine reduces oxidative damage or delays senescence of the cells.

5

10